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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/781,712	02/12/2001	Stanley T. Crooke	ISPH-0520	2237
26259	7590	10/06/2004	EXAMINER	
LICATLA & TYRRELL P.C. 66 E. MAIN STREET MARLTON, NJ 08053			SCHULTZ, JAMES	
			ART UNIT	PAPER NUMBER
			1635	
DATE MAILED: 10/06/2004				

Please find below and/or attached an Office communication concerning this application or proceeding.

## Office Action Summary

Application No.

09/781,712

Applicant(s)

CROOKE ET AL.

Examiner

J. D. Schultz, Ph.D.

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 1 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 12 February 2001.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 1-66 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☐ Claim(s) \_\_\_\_\_ is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☒ Claim(s) 1-66 are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
  - ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

- |  |   |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)   | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)                                   | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152)             |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)<br>Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____  |

*Election/Restrictions*

1. Restriction to one of the following inventions is required under 35 U.S.C. 121:

I. Claims 2, 3, 5-9, 13, 14, and 16-20 are drawn to a method of promoting inhibition of expression of a selected protein or eliciting cleavage of an RNA encoding said protein, comprising incubating an antisense oligo with a mammalian or human RNase HI polypeptide such that cleavage results, classified for example in class 514, subclass 44.

Election of this group requires further election of a single sequence as described below.

II. Claims 2, 4-7, 10, 13, 15-18, 21, 22, drawn to a method of promoting inhibition of expression of a selected protein or eliciting cleavage of an RNA encoding said protein, comprising incubating an antisense oligo with a mammalian or human RNase HII polypeptide such that cleavage results, classified in class 514, subclass 44.

Election of this group requires further election of a single sequence as described below.

III. Claims 24-27 and 29-35 drawn to a method of screening for effective antisense oligos comprising administering a mammalian or human RNase HI or HII with an RNA duplex comprising an antisense hybridized to its target, allowing cleavage to take place, and determining where on the target cleavage occurred to identify a site that is RNase H sensitive, classified for example in class 435, subclass 6.

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- IV. Claims 24-26, 28, and 29-35 drawn to a method of screening for effective antisense oligos comprising administering a mammalian RNase HI or HII with an RNA duplex comprising an antisense hybridized to its target, allowing cleavage to take place, and determining where on the target cleavage occurred to identify a site that is RNase H sensitive, classified for example in class 435, subclass 6.
- V. Claim 37, drawn to a method of prognosticating efficacy of antisense therapy of a selected disease comprising measuring the level or activity of a human RNase HI polypeptide in a target cell, classified for example in class 435, subclass 4.
- VI. Claim 38, drawn to a method of prognosticating efficacy of antisense therapy of a selected disease comprising measuring the level or activity of a human RNase HII polypeptide in a target cell, classified for example in class 435, subclass 4.
- VII. Claims 40 and 41, drawn to a method of identifying agents which increase or decrease activity of a mammalian or human RNase HI polypeptide, classified for example in class 435, subclass 6.
- VIII. Claims 40 and 42, drawn to a method of identifying agents which increase or decrease activity of a mammalian or human RNase HII polypeptide, classified for example in class 435, subclass 6.
- IX. Claims 43-45, drawn to an isolated human RNase HII polypeptide comprising SEQ ID NO: 1 or that deposited at ATCC No. PTA-2897, Classified for example in class 435, subclass 199.

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- X. Claims 46-50, drawn to an isolated human RNase HII polynucleotide comprising SEQ ID NO: 12 or that deposited at ATCC No. PTA-2897, and vectors and cells thereto, classified for example in class 435, subclass 199.
- XI. Claim 51, drawn to an antibody targeted to a human RNase HII, classified in class 530, subclass 387.1.
- XII. Claims 52, and 54-64 drawn to nucleic acid probes and antisense oligos directed to human RNase HII, and modifications thereof, classified, for example, in class 536, subclass 24.5.  
Election of this group requires further election of a single sequence as described below.
- XIII. Claims 65 and 66, drawn to methods of inhibiting human RNase HII polypeptide expression comprising administering an oligo targeted at a polynucleotide that encodes said polypeptide, targeted for example in class 514, subclass 44.

2. Claims 1 and 12 link(s) the inventions of Groups I and II. Furthermore, claim 23 links the inventions of groups III and IV, claim 36 links the inventions of Groups V and VI, claim 39 links the invention of groups VII and VIII, and claim 53 links XII and XIII. The restriction requirement between the linked inventions is subject to the nonallowance of the linking claim(s), claims 1, 12, 23, 36, 39 and 53. Upon the allowance of the linking claim(s), the restriction requirement as to the linked inventions shall be withdrawn and any claim(s) depending from or otherwise including all the limitations of the allowable linking claim(s) will be entitled to examination in the instant application. Applicant(s) are advised that if any such claim(s)

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depending from or including all the limitations of the allowable linking claim(s) is/are presented in a continuation or divisional application, the claims of the continuation or divisional application may be subject to provisional statutory and/or nonstatutory double patenting rejections over the claims of the instant application. Where a restriction requirement is withdrawn, the provisions of 35 U.S.C. 121 are no longer applicable. *In re Ziegler*, 44 F.2d 1211, 1215, 170 USPQ 129, 131-32 (CCPA 1971). See also MPEP § 804.01.

3. The inventions are distinct, each from the other because of the following reasons:

Inventions I and II are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case the different inventions are unrelated because they have different modes of operation, since Group I uses RNase HI, and Group II uses RNase HII, which are different compounds. Thus the methods have different modes of operation. Furthermore, the methods of these Groups are not disclosed as useful together. Finally, to search and examine methods involving separate, distinct sequences that have different structures requires searches that are divergent and do not overlap, which is considered a burden. Restriction is considered proper therefore.

Inventions I and III are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case the different inventions are not related because the invention of Group III requires determining sites of cleavage upon the target RNA, which is not required of Group I. Thus, the Groups have different modes of operation, and since they are not disclosed as useful together, these Groups are

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considered patentably distinct. Because these inventions are distinct for the reasons given above and the search required for Group I is not required for Group III because each group contains unique steps absent in the other Group, and because the search for multiple methods comprising different steps is considered burdensome, and restriction for examination purposes as indicated is proper.

Inventions II and III are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case the different inventions are not related because the invention of Group III requires determining sites of cleavage upon the target RNA, which is not required of Group II. Thus, the Groups have different modes of operation, and since they are not disclosed as useful together, these Groups are considered patentably distinct. Because these inventions are distinct for the reasons given above and the search required for Group II is not required for Group IV because each group contains unique steps absent in the other Group, and because the search for multiple methods comprising different steps is considered burdensome, and restriction for examination purposes as indicated is proper.

Inventions I and IV are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case the different inventions are not related because the invention of Group IV requires determining sites of cleavage upon the target RNA, which is not required of Group I. Thus, the Groups have different modes of operation, and since they are not disclosed as useful together, these Groups are

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considered patentably distinct. Because these inventions are distinct for the reasons given above and the search required for Group I is not required for Group IV because each group contains unique steps absent in the other Group, and because the search for multiple methods comprising different steps is considered burdensome, and restriction for examination purposes as indicated is proper.

Inventions II and IV are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case the different inventions are not related because the invention of Group IV requires determining sites of cleavage upon the target RNA, which is not required of Group II. Thus, the Groups have different modes of operation, and since they are not disclosed as useful together, these Groups are considered patentably distinct. Because these inventions are distinct for the reasons given above and the search required for Group II is not required for Group IV because each group contains unique steps absent in the other Group, and because the search for multiple methods comprising different steps is considered burdensome, and restriction for examination purposes as indicated is proper.

Inventions III and IV are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case the different inventions are unrelated because they have different modes of operation, since Group III uses RNase HI, and Group IV uses RNase HII, which are different compounds. Thus the methods have different modes of operation. Furthermore, the methods of each Group are not disclosed as



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useful together. Finally, to search and examine methods involving separate, distinct sequences that have different structures requires searches that are divergent and do not overlap, which is considered a burden. Restriction is considered proper therefore.

Inventions I and V are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case the different inventions are not related because the invention of Group V requires determining the specific activity level of RNase HI, which is not required of Group I. Thus, the Groups have different modes of operation, and since they are not disclosed as useful together, these Groups are considered patentably distinct. Because these inventions are distinct for the reasons given above and the search required for Group I is not required for Group V because each group contains unique steps absent in the other Group, and because the search for multiple methods comprising different steps is considered burdensome, and restriction for examination purposes as indicated is proper.

Inventions II and V are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case the different inventions are not related because the invention of Group V requires determining the specific activity level of RNase HI, which is not required of Group II. Thus, the Groups have different modes of operation, and since they are not disclosed as useful together, these Groups are considered patentably distinct. Because these inventions are distinct for the reasons given above and the search required for Group II is not required for Group V because each group contains

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unique steps absent in the other Group, and because the search for multiple methods comprising different steps is considered burdensome, and restriction for examination purposes as indicated is proper.

Inventions III and V are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case the different inventions are not related because the invention of Group V requires determining the specific activity level of RNase HI, which is not required of Group III. Thus, the Groups have different modes of operation, and since they are not disclosed as useful together, these Groups are considered patentably distinct. Because these inventions are distinct for the reasons given above and the search required for Group III is not required for Group V because each group contains unique steps absent in the other Group, and because the search for multiple methods comprising different steps is considered burdensome, and restriction for examination purposes as indicated is proper.

Inventions IV and V are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case the different inventions are not related because the invention of Group V requires determining the specific activity level of RNase HI, which is not required of Group IV. Thus, the Groups have different modes of operation, and since they are not disclosed as useful together, these Groups are considered patentably distinct. Because these inventions are distinct for the reasons given above and the search required for Group IV is not required for Group V because each group contains

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unique steps absent in the other Group, and because the search for multiple methods comprising different steps is considered burdensome, and restriction for examination purposes as indicated is proper.

Inventions I and VI are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case the different inventions are not related because the invention of Group VI requires determining the specific activity level of RNase HIII, which is not required of Group I. Thus, the Groups have different modes of operation, and since they are not disclosed as useful together, these Groups are considered patentably distinct. Because these inventions are distinct for the reasons given above and the search required for Group I is not required for Group VI because each group contains unique steps absent in the other Group, and because the search for multiple methods comprising different steps is considered burdensome, and restriction for examination purposes as indicated is proper.

Inventions II and VI are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case the different inventions are not related because the invention of Group VI requires determining the specific activity level of RNase HIII, which is not required of Group II. Thus, the Groups have different modes of operation, and since they are not disclosed as useful together, these Groups are considered patentably distinct. Because these inventions are distinct for the reasons given above and the search required for Group II is not required for Group VI because each group contains

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unique steps absent in the other Group, and because the search for multiple methods comprising different steps is considered burdensome, and restriction for examination purposes as indicated is proper.

Inventions III and VI are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case the different inventions are not related because the invention of Group VI requires determining the specific activity level of RNase HII, which is not required of Group III. Thus, the Groups have different modes of operation, and since they are not disclosed as useful together, these Groups are considered patentably distinct. Because these inventions are distinct for the reasons given above and the search required for Group III is not required for Group VI because each group contains unique steps absent in the other Group, and because the search for multiple methods comprising different steps is considered burdensome, and restriction for examination purposes as indicated is proper.

Inventions IV and VI are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case the different inventions are not related because the invention of Group VI requires determining the specific activity level of RNase HII, which is not required of Group IV. Thus, the Groups have different modes of operation, and since they are not disclosed as useful together, these Groups are considered patentably distinct. Because these inventions are distinct for the reasons given above and the search required for Group IV is not required for Group VI because each group contains

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unique steps absent in the other Group, and because the search for multiple methods comprising different steps is considered burdensome, and restriction for examination purposes as indicated is proper.

Inventions V and VI are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case the different inventions are unrelated because they have different modes of operation, since Group V uses RNase HI, and Group VI uses RNase HII, which are different compounds. Thus the methods have different modes of operation. Furthermore, the methods of these Groups are not disclosed as useful together. Finally, to search and examine methods involving separate, distinct sequences that have different structures requires searches that are divergent and do not overlap, which is considered a burden. Restriction is considered proper therefore.

Inventions I and VII are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case the different inventions are not related because the invention of Group VII requires administering multiple test compounds and then subsequently determining whether the compound has an effect on the specific activity level of RNase HI, which is not required of Group I. Thus, the Groups have different modes of operation, and since they are not disclosed as useful together, these Groups are considered patentably distinct. Because these inventions are distinct for the reasons given above and the search required for one Group is not required for the other Group because each group contains unique steps absent in the other Group, and because the search for multiple

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methods comprising different steps is considered burdensome, restriction for examination purposes as indicated is proper.

Inventions II and VII are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case the different inventions are not related because the invention of Group VII requires administering multiple test compounds and then subsequently determining whether the compound has an effect on the specific activity level of RNase HI, which is not required of Group II. Thus, the Groups have different modes of operation, and since they are not disclosed as useful together, these Groups are considered patentably distinct. Because these inventions are distinct for the reasons given above and the search required for one Group is not required for the other Group because each group contains unique steps absent in the other Group, and because the search for multiple methods comprising different steps is considered burdensome, restriction for examination purposes as indicated is proper.

Inventions III and VII are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case the different inventions are not related because the invention of Group VII requires administering multiple test compounds and then subsequently determining whether the compound has an effect on the specific activity level of RNase HI, which is not required of Group III. Thus, the Groups have different modes of operation, and since they are not disclosed as useful together, these Groups are considered patentably distinct. Because these inventions are distinct for the reasons given

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above and the search required for one Group is not required for the other Group because each group contains unique steps absent in the other Group, and because the search for multiple methods comprising different steps is considered burdensome, restriction for examination purposes as indicated is proper.

Inventions IV and VII are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case the different inventions are not related because the invention of Group VII requires administering multiple test compounds and then subsequently determining whether the compound has an effect on the specific activity level of RNase HI, which is not required of Group IV. Thus, the Groups have different modes of operation, and since they are not disclosed as useful together, these Groups are considered patentably distinct. Because these inventions are distinct for the reasons given above and the search required for one Group is not required for the other Group because each group contains unique steps absent in the other Group, and because the search for multiple methods comprising different steps is considered burdensome, restriction for examination purposes as indicated is proper.

Inventions V and VII are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case the different inventions are not related because the invention of Group VII requires administering multiple test compounds and then subsequently determining whether the compound has an effect on the specific activity level of RNase HI, which is not required of Group V. Thus, the Groups have

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different modes of operation, and since they are not disclosed as useful together, these Groups are considered patentably distinct. Because these inventions are distinct for the reasons given above and the search required for one Group is not required for the other Group because each group contains unique steps absent in the other Group, and because the search for multiple methods comprising different steps is considered burdensome, restriction for examination purposes as indicated is proper.

Inventions VI and VII are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case the different inventions are not related because the invention of Group VII requires administering multiple test compounds and then subsequently determining whether the compound has an effect on the specific activity level of RNase HI, which is not required of Group VI. Thus, the Groups have different modes of operation, and since they are not disclosed as useful together, these Groups are considered patentably distinct. Because these inventions are distinct for the reasons given above and the search required for one Group is not required for the other Group because each group contains unique steps absent in the other Group, and because the search for multiple methods comprising different steps is considered burdensome, restriction for examination purposes as indicated is proper.

Inventions I and VIII are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case the different inventions are not related because the invention of Group VIII requires administering multiple



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test compounds and then subsequently determining whether the compound has an effect on the specific activity level of RNase HII, which is not required of Group I. Thus, the Groups have different modes of operation, and since they are not disclosed as useful together, these Groups are considered patentably distinct. Because these inventions are distinct for the reasons given above and the search required for one Group is not required for the other Group because each group contains unique steps absent in the other Group, and because the search for multiple methods comprising different steps is considered burdensome, restriction for examination purposes as indicated is proper.

Inventions II and VIII are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case the different inventions are not related because the invention of Group VIII requires administering multiple test compounds and then subsequently determining whether the compound has an effect on the specific activity level of RNase HII, which is not required of Group II. Thus, the Groups have different modes of operation, and since they are not disclosed as useful together, these Groups are considered patentably distinct. Because these inventions are distinct for the reasons given above and the search required for one Group is not required for the other Group because each group contains unique steps absent in the other Group, and because the search for multiple methods comprising different steps is considered burdensome, restriction for examination purposes as indicated is proper.

Inventions III and VIII are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation,

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different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case the different inventions are not related because the invention of Group VIII requires administering multiple test compounds and then subsequently determining whether the compound has an effect on the specific activity level of RNase HII, which is not required of Group III. Thus, the Groups have different modes of operation, and since they are not disclosed as useful together, these Groups are considered patentably distinct. Because these inventions are distinct for the reasons given above and the search required for one Group is not required for the other Group because each group contains unique steps absent in the other Group, and because the search for multiple methods comprising different steps is considered burdensome, restriction for examination purposes as indicated is proper.

Inventions IV and VIII are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case the different inventions are not related because the invention of Group VIII requires administering multiple test compounds and then subsequently determining whether the compound has an effect on the specific activity level of RNase HII, which is not required of Group IV. Thus, the Groups have different modes of operation, and since they are not disclosed as useful together, these Groups are considered patentably distinct. Because these inventions are distinct for the reasons given above and the search required for one Group is not required for the other Group because each group contains unique steps absent in the other Group, and because the search for multiple methods comprising different steps is considered burdensome, restriction for examination purposes as indicated is proper.

Inventions V and VIII are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case the different inventions are not related because the invention of Group VIII requires administering multiple test compounds and then subsequently determining whether the compound has an effect on the specific activity level of RNase HII, which is not required of Group V. Thus, the Groups have different modes of operation, and since they are not disclosed as useful together, these Groups are considered patentably distinct. Because these inventions are distinct for the reasons given above and the search required for one Group is not required for the other Group because each group contains unique steps absent in the other Group, and because the search for multiple methods comprising different steps is considered burdensome, restriction for examination purposes as indicated is proper.

Inventions VI and VIII are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case the different inventions are not related because the invention of Group VIII requires administering multiple test compounds and then subsequently determining whether the compound has an effect on the specific activity level of RNase HII, which is not required of Group VI. Thus, the Groups have different modes of operation, and since they are not disclosed as useful together, these Groups are considered patentably distinct. Because these inventions are distinct for the reasons given above and the search required for one Group is not required for the other Group because each group contains unique steps absent in the other Group, and because the search for multiple

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methods comprising different steps is considered burdensome, restriction for examination purposes as indicated is proper.

Inventions VII and VIII are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case the different inventions are unrelated because they have different modes of operation, since Group VII uses RNase HI, and Group VIII uses RNase HII, which are different compounds. Thus the methods have different modes of operation. Furthermore, the methods of these Groups are not disclosed as useful together. Finally, to search and examine methods involving separate, distinct sequences that have different structures requires searches that are divergent and do not overlap, which is considered a burden. Restriction is considered proper therefore.

Inventions I and IX are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case the different inventions are unrelated because the invention of Group I is drawn to the use of a different compound, i.e. RNase HI, than that contained in Group IX. Thus the Groups have different modes of operation. Furthermore, the methods of these Groups are not disclosed as useful together. Finally, to search and examine Groups involving separate, distinct sequences that have different structures requires searches that are divergent and do not overlap, which is considered a burden. Restriction is considered proper therefore.

Inventions II and IX are related as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the

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product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product (MPEP § 806.05(h)). In the instant case the product as claimed can be used in a materially different process of using that product, for example in searching for inhibitors of RNase HII, such as those set forth in claim 42. Furthermore, it is a burden to search and examine Groups involving methods which depend upon a series of separate molecules, such as the antisense oligos required in the method of Group II, because the searches that are divergent and do not overlap. Restriction is considered proper therefore.

Inventions III and IX are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case the different inventions are unrelated because the invention of Group III is drawn to the use of a different compound, i.e. RNase HI, than that contained in Group IX. Thus the Groups have different modes of operation. Furthermore, the methods of these Groups are not disclosed as useful together. Finally, to search and examine Groups involving separate, distinct sequences that have different structures requires searches that are divergent and do not overlap, which is considered a burden. Restriction is considered proper therefore.

Inventions IV and IX are related as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product (MPEP § 806.05(h)). In the instant case the product as claimed can be used in a materially different

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process of using that product, for example in searching for inhibitors of RNase HII, such as those set forth in claim 42. Furthermore, it is a burden to search and examine Groups involving methods which depend upon a series of separate molecules, such as the antisense oligos required in the method of Group IV, because the searches that are divergent and do not overlap.

Restriction is considered proper therefore.

Inventions V and IX are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case the different inventions are unrelated because the invention of Group V is drawn to the use of a different compound, i.e. RNase HI, than that contained in Group IX. Thus the Groups have different modes of operation. Furthermore, the methods of these Groups are not disclosed as useful together. Finally, to search and examine Groups involving separate, distinct sequences that have different structures requires searches that are divergent and do not overlap, which is considered a burden. Restriction is considered proper therefore.

Inventions VI and IX are related as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product (MPEP § 806.05(h)). In the instant case the product as claimed can be used in a materially different process of using that product, for example in searching for inhibitors of RNase HII, such as those set forth in claim 42. Furthermore, it is a burden to search and examine Groups involving methods which depend upon a series of separate molecules, such as the antisense oligos required

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in the method of Group VI, because the searches that are divergent and do not overlap.

Restriction is considered proper therefore.

Inventions VII and IX are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case the different inventions are unrelated because the invention of Group VII is drawn to the use of a different compound, i.e. RNase HI, than that contained in Group IX. Thus the Groups have different modes of operation. Furthermore, the methods of these Groups are not disclosed as useful together. Finally, to search and examine Groups involving separate, distinct sequences that have different structures requires searches that are divergent and do not overlap, which is considered a burden. Restriction is considered proper therefore.

Inventions VIII and IX are related as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product (MPEP § 806.05(h)). In the instant case the product as claimed can be used in a materially different process of using that product, for example in enhancing the cleavage of a target utilizing RNase HII, such as those set forth in claim 4. Furthermore, it is a burden to search and examine Groups involving methods which depend upon a series of separate molecules, such as the antisense oligos required in the method of Group VIII, because the searches that are divergent and do not overlap. Restriction is considered proper therefore.

Inventions I and X are unrelated to each other. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case the inventions differ in that one is drawn to a method while the other is drawn to a compound, and furthermore, because the method does not utilize the compound of the instant method. Thus, the Groups are patentably distinct because they have different modes of operation and different effects, and are not disclosed as capable of use together. Furthermore, it is a burden to search and examine Groups involving both compounds and methods which are not used together in a disclosed method, and further because the searches are divergent and do not overlap. Restriction is considered proper therefore.

Inventions II and X are unrelated to each other. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case the inventions differ in that one is drawn to a method while the other is drawn to a compound, and furthermore, because the method does not utilize the compound of the instant method. Thus, the Groups are patentably distinct because they have different modes of operation and different effects, and are not disclosed as capable of use together. Furthermore, it is a burden to search and examine Groups involving both compounds and methods which are not used together in a disclosed method, and further because the searches are divergent and do not overlap. Restriction is considered proper therefore.

Inventions III and X are unrelated to each other. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of



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operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case the inventions differ in that one is drawn to a method while the other is drawn to a compound, and furthermore, because the method does not utilize the compound of the instant method. Thus, the Groups are patentably distinct because they have different modes of operation and different effects, and are not disclosed as capable of use together. Furthermore, it is a burden to search and examine Groups involving both compounds and methods which are not used together in a disclosed method, and further because the searches are divergent and do not overlap. Restriction is considered proper therefore.

Inventions IV and X are unrelated to each other. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case the inventions differ in that one is drawn to a method while the other is drawn to a compound, and furthermore, because the method does not utilize the compound of the instant method. Thus, the Groups are patentably distinct because they have different modes of operation and different effects, and are not disclosed as capable of use together. Furthermore, it is a burden to search and examine Groups involving both compounds and methods which are not used together in a disclosed method, and further because the searches are divergent and do not overlap. Restriction is considered proper therefore.

Inventions V and X are unrelated to each other. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case the inventions differ in that one is drawn to a method while the other is drawn to a

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compound, and furthermore, because the method does not utilize the compound of the instant method. Thus, the Groups are patentably distinct because they have different modes of operation and different effects, and are not disclosed as capable of use together. Furthermore, it is a burden to search and examine Groups involving both compounds and methods which are not used together in a disclosed method, and further because the searches are divergent and do not overlap. Restriction is considered proper therefore.

Inventions VI and X are unrelated to each other. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case the inventions differ in that one is drawn to a method while the other is drawn to a compound, and furthermore, because the method does not utilize the compound of the instant method. Thus, the Groups are patentably distinct because they have different modes of operation and different effects, and are not disclosed as capable of use together. Furthermore, it is a burden to search and examine Groups involving both compounds and methods which are not used together in a disclosed method, and further because the searches are divergent and do not overlap. Restriction is considered proper therefore.

Inventions VII and X are unrelated to each other. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case the inventions differ in that one is drawn to a method while the other is drawn to a compound, and furthermore, because the method does not utilize the compound of the instant method. Thus, the Groups are patentably distinct because they have different modes of operation

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and different effects, and are not disclosed as capable of use together. Furthermore, it is a burden to search and examine Groups involving both compounds and methods which are not used together in a disclosed method, and further because the searches are divergent and do not overlap. Restriction is considered proper therefore.

Inventions VIII and X are unrelated to each other. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case the inventions differ in that one is drawn to a method while the other is drawn to a compound, and furthermore, because the method does not utilize the compound of the instant method. Thus, the Groups are patentably distinct because they have different modes of operation and different effects, and are not disclosed as capable of use together. Furthermore, it is a burden to search and examine Groups involving both compounds and methods which are not used together in a disclosed method, and further because the searches are divergent and do not overlap. Restriction is considered proper therefore.

Inventions IX and X are unrelated to each other. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case the different inventions each comprise chemical structures that are independent of one another and not disclosed as capable of use together, and thus have different modes of operation. The polypeptide of Group IX is not disclosed as being used in any method with either the polynucleotide of Group X. Furthermore, it is a burden to search and examine Groups involving compounds which are distinct because a separate search must be run for both, and

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further because the searches are divergent and do not necessarily overlap. Restriction is considered proper therefore.

Inventions I and XI are unrelated to each other. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case the inventions differ in that one is drawn to an antibody, while the other is drawn to a method, and furthermore, because the method does not utilize the compound of the instant method. Thus, the Groups are patentably distinct because they have different modes of operation and different effects, and are not disclosed as capable of use together. Furthermore, it is a burden to search and examine Groups involving both compounds and methods which are not used together in a disclosed method, and further because the searches are divergent and do not overlap. Restriction is considered proper therefore.

Inventions II and XI are unrelated to each other. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case the inventions differ in that one is drawn to an antibody, while the other is drawn to a method, and furthermore, because the method does not utilize the compound of the instant method. Thus, the Groups are patentably distinct because they have different modes of operation and different effects, and are not disclosed as capable of use together. Furthermore, it is a burden to search and examine Groups involving both compounds and methods which are not used together in a disclosed method, and further because the searches are divergent and do not overlap. Restriction is considered proper therefore.

Inventions III and XI are unrelated to each other. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case the inventions differ in that one is drawn to an antibody, while the other is drawn to a method, and furthermore, because the method does not utilize the compound of the instant method. Thus, the Groups are patentably distinct because they have different modes of operation and different effects, and are not disclosed as capable of use together. Furthermore, it is a burden to search and examine Groups involving both compounds and methods which are not used together in a disclosed method, and further because the searches are divergent and do not overlap. Restriction is considered proper therefore.

Inventions IV and XI are unrelated to each other. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case the inventions differ in that one is drawn to an antibody, while the other is drawn to a method, and furthermore, because the method does not utilize the compound of the instant method. Thus, the Groups are patentably distinct because they have different modes of operation and different effects, and are not disclosed as capable of use together. Furthermore, it is a burden to search and examine Groups involving both compounds and methods which are not used together in a disclosed method, and further because the searches are divergent and do not overlap. Restriction is considered proper therefore.

Inventions V and XI are unrelated to each other. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of

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operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case the inventions differ in that one is drawn to an antibody, while the other is drawn to a method, and furthermore, because the method does not utilize the compound of the instant method. Thus, the Groups are patentably distinct because they have different modes of operation and different effects, and are not disclosed as capable of use together. Furthermore, it is a burden to search and examine Groups involving both compounds and methods which are not used together in a disclosed method, and further because the searches are divergent and do not overlap. Restriction is considered proper therefore.

Inventions VI and XI are unrelated to each other. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case the inventions differ in that one is drawn to an antibody, while the other is drawn to a method, and furthermore, because the method does not utilize the compound of the instant method. Thus, the Groups are patentably distinct because they have different modes of operation and different effects, and are not disclosed as capable of use together. Furthermore, it is a burden to search and examine Groups involving both compounds and methods which are not used together in a disclosed method, and further because the searches are divergent and do not overlap. Restriction is considered proper therefore.

Inventions VII and XI are unrelated to each other. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case the inventions differ in that one is drawn to an antibody, while the other is drawn to a

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method, and furthermore, because the method does not utilize the compound of the instant method. Thus, the Groups are patentably distinct because they have different modes of operation and different effects, and are not disclosed as capable of use together. Furthermore, it is a burden to search and examine Groups involving both compounds and methods which are not used together in a disclosed method, and further because the searches are divergent and do not overlap. Restriction is considered proper therefore.

Inventions VIII and XI are unrelated to each other. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case the inventions differ in that one is drawn to an antibody, while the other is drawn to a method, and furthermore, because the method does not utilize the compound of the instant method. Thus, the Groups are patentably distinct because they have different modes of operation and different effects, and are not disclosed as capable of use together. Furthermore, it is a burden to search and examine Groups involving both compounds and methods which are not used together in a disclosed method, and further because the searches are divergent and do not overlap. Restriction is considered proper therefore.

Inventions IX and XI are unrelated to each other. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case the different inventions each comprise chemical structures that are independent of one another and not disclosed as capable of use together, and thus have different modes of operation. Furthermore, it is a burden to search and examine Groups involving compounds which

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are distinct because a separate search must be run for both, and further because the searches are divergent and do not necessarily overlap. Restriction is considered proper therefore.

Inventions X and XI are unrelated to each other. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case the different inventions each comprise chemical structures that are independent of one another and not disclosed as capable of use together, and thus have different modes of operation. Furthermore, the polynucleotide of Group X is not disclosed as being used in any method with either the antibody of Group XI. Furthermore, it is a burden to search and examine Groups involving compounds which are distinct because a separate search must be run for both, and further because the searches are divergent and do not necessarily overlap. Restriction is considered proper therefore.

Inventions I and XII are unrelated to each other. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case the inventions differ in that one is drawn to an probe, while the other is drawn to a method, and furthermore, because the method does not utilize the compound of the instant method. Thus, the Groups are patentably distinct because they have different modes of operation and different effects, and are not disclosed as capable of use together. Furthermore, it is a burden to search and examine Groups involving both compounds and methods which are not used together in a disclosed method, and further because the searches are divergent and do not overlap. Restriction is considered proper therefore.



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Inventions II and XII are unrelated to each other. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case the inventions differ in that one is drawn to an probe, while the other is drawn to a method, and furthermore, because the method does not utilize the compound of the instant method. Thus, the Groups are patentably distinct because they have different modes of operation and different effects, and are not disclosed as capable of use together. Furthermore, it is a burden to search and examine Groups involving both compounds and methods which are not used together in a disclosed method, and further because the searches are divergent and do not overlap. Restriction is considered proper therefore.

Inventions III and XII are unrelated to each other. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case the inventions differ in that one is drawn to an probe, while the other is drawn to a method, and furthermore, because the method does not utilize the compound of the instant method. Thus, the Groups are patentably distinct because they have different modes of operation and different effects, and are not disclosed as capable of use together. Furthermore, it is a burden to search and examine Groups involving both compounds and methods which are not used together in a disclosed method, and further because the searches are divergent and do not overlap. Restriction is considered proper therefore.

Inventions IV and XII are unrelated to each other. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of

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operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case the inventions differ in that one is drawn to an probe, while the other is drawn to a method, and furthermore, because the method does not utilize the compound of the instant method. Thus, the Groups are patentably distinct because they have different modes of operation and different effects, and are not disclosed as capable of use together. Furthermore, it is a burden to search and examine Groups involving both compounds and methods which are not used together in a disclosed method, and further because the searches are divergent and do not overlap. Restriction is considered proper therefore.

Inventions V and XII are unrelated to each other. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case the inventions differ in that one is drawn to an probe, while the other is drawn to a method, and furthermore, because the method does not utilize the compound of the instant method. Thus, the Groups are patentably distinct because they have different modes of operation and different effects, and are not disclosed as capable of use together. Furthermore, it is a burden to search and examine Groups involving both compounds and methods which are not used together in a disclosed method, and further because the searches are divergent and do not overlap. Restriction is considered proper therefore.

Inventions VI and XII are unrelated to each other. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case the inventions differ in that one is drawn to an probe, while the other is drawn to a

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method, and furthermore, because the method does not utilize the compound of the instant method. Thus, the Groups are patentably distinct because they have different modes of operation and different effects, and are not disclosed as capable of use together. Furthermore, it is a burden to search and examine Groups involving both compounds and methods which are not used together in a disclosed method, and further because the searches are divergent and do not overlap. Restriction is considered proper therefore.

Inventions VII and XII are unrelated to each other. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case the inventions differ in that one is drawn to an probe, while the other is drawn to a method, and furthermore, because the method does not utilize the compound of the instant method. Thus, the Groups are patentably distinct because they have different modes of operation and different effects, and are not disclosed as capable of use together. Furthermore, it is a burden to search and examine Groups involving both compounds and methods which are not used together in a disclosed method, and further because the searches are divergent and do not overlap. Restriction is considered proper therefore.

Inventions VIII and XII are unrelated to each other. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case the inventions differ in that one is drawn to an probe, while the other is drawn to a method, and furthermore, because the method does not utilize the compound of the instant method. Thus, the Groups are patentably distinct because they have different modes of operation

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and different effects, and are not disclosed as capable of use together. Finally, it is a burden to search and examine Groups involving both compounds and methods which are not used together in a disclosed method, and further because the searches are divergent and do not overlap.

Restriction is considered proper therefore.

Inventions IX and XII are unrelated to each other. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case the different inventions each comprise chemical structures that are independent of one another and not disclosed as capable of use together, and thus have different modes of operation. Furthermore, the polypeptide of Group IX is not disclosed as being used in any method with either the probe or antisense of Group XI. Finally, it is a burden to search and examine Groups involving compounds which are distinct because a separate search must be run for both, and further because the searches are divergent and do not necessarily overlap.

Restriction is considered proper therefore.

Inventions X and XII are unrelated to each other. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case the different inventions each comprise chemical structures, i.e. different sequences that are independent of one another and not disclosed as capable of use together, and thus have different modes of operation. Finally, it is a burden to search and examine Groups involving compounds which are distinct because a separate search must be run for both, and further because the searches are divergent and do not necessarily overlap.

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Inventions XI and XII are unrelated to each other. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case the different inventions each comprise chemical structures, i.e. different sequences, that are independent of one another, and thus have different modes of operation. Finally, it is a burden to search and examine Groups involving compounds which are distinct because a separate search must be run for both, and further because the searches are divergent and do not necessarily overlap.

Inventions I and XIII are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case the different inventions are unrelated because Group XIII requires the administration of a single oligo directed to the inhibition of RNase HII for therapeutic end, which is not required of any other group. Thus, the Groups are patentably distinct because they have different modes of operation and different effects, and are not disclosed as capable of use together. Finally, it is a burden to search and examine Groups involving methods which contain distinct and disparate steps, and further because the searches are divergent and do not overlap. Restriction is considered proper therefore.

Inventions II and XIII are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case the different inventions are unrelated because Group XIII requires the administration of a single oligo directed to the inhibition of RNase HII for therapeutic end, which is not required of any other group.

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Thus, the Groups are patentably distinct because they have different modes of operation and different effects, and are not disclosed as capable of use together. Finally, it is a burden to search and examine Groups involving methods which contain distinct and disparate steps, and further because the searches are divergent and do not overlap. Restriction is considered proper therefore.

Inventions III and XIII are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case the different inventions are unrelated because Group XIII requires the administration of a single oligo directed to the inhibition of RNase HII for therapeutic end, which is not required of any other group. Thus, the Groups are patentably distinct because they have different modes of operation and different effects, and are not disclosed as capable of use together. Finally, it is a burden to search and examine Groups involving methods which contain distinct and disparate steps, and further because the searches are divergent and do not overlap. Restriction is considered proper therefore.

Inventions IV and XIII are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case the different inventions are unrelated because Group XIII requires the administration of a single oligo directed to the inhibition of RNase HII for therapeutic end, which is not required of any other group. Thus, the Groups are patentably distinct because they have different modes of operation and different effects, and are not disclosed as capable of use together. Finally, it is a burden to search and examine Groups involving methods which contain distinct and disparate

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steps, and further because the searches are divergent and do not overlap. Restriction is considered proper therefore.

Inventions V and XIII are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case the different inventions are unrelated because Group XIII requires the administration of a single oligo directed to the inhibition of RNase HII for therapeutic end, which is not required of any other group. Thus, the Groups are patentably distinct because they have different modes of operation and different effects, and are not disclosed as capable of use together. Finally, it is a burden to search and examine Groups involving methods which contain distinct and disparate steps, and further because the searches are divergent and do not overlap. Restriction is considered proper therefore.

Inventions VI and XIII are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case the different inventions are unrelated because Group XIII requires the administration of a single oligo directed to the inhibition of RNase HII for therapeutic end, which is not required of any other group. Thus, the Groups are patentably distinct because they have different modes of operation and different effects, and are not disclosed as capable of use together. Finally, it is a burden to search and examine Groups involving methods which contain distinct and disparate steps, and further because the searches are divergent and do not overlap. Restriction is considered proper therefore.

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Inventions VII and XIII are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case the different inventions are unrelated because Group XIII requires the administration of a single oligo directed to the inhibition of RNase HII for therapeutic end, which is not required of any other group. Thus, the Groups are patentably distinct because they have different modes of operation and different effects, and are not disclosed as capable of use together. Finally, it is a burden to search and examine Groups involving methods which contain distinct and disparate steps, and further because the searches are divergent and do not overlap. Restriction is considered proper therefore.

Inventions VIII and XIII are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case the different inventions are unrelated because Group XIII requires the administration of a single oligo directed to the inhibition of RNase HII for therapeutic end, which is not required of any other group. Thus, the Groups are patentably distinct because they have different modes of operation and different effects, and are not disclosed as capable of use together. Finally, it is a burden to search and examine Groups involving methods which contain distinct and disparate steps, and further because the searches are divergent and do not overlap. Restriction is considered proper therefore.

Inventions IX and XIII are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation,



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different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case the different inventions are unrelated because the invention of Group IX is drawn to the polypeptide compound, while the method of Group XIII is drawn to the cleavage of the polynucleotide of Group X, and therefore the instant method does not use or refer to the instant compound. They are thus not disclosed as useful together, and have different modes of operation, different functions, and different effects. Finally, it is a burden to search and examine Groups involving both compounds and methods which are not used together in a disclosed method, and further because the searches are divergent and do not overlap. Restriction is considered proper therefore.

Inventions X and XIII are related as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product (MPEP § 806.05(h)). In the instant case the polynucleotide of Group X can be used to express the polypeptide product, RNase HII. Furthermore, it is a burden to search and examine Groups that are drawn to materially different entities (i.e. methods and compounds), because one contains an active process while the other is defined by its structure, and further because the searches are divergent and do not necessarily overlap. Restriction is considered proper therefore.

Inventions XI and XIII are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case the different inventions are unrelated because the invention of Group IX is drawn to an antibody directed to RNase HII, while the method of Group XIII is drawn to the cleavage of the

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polynucleotide of Group X, and therefore the instant method does not use or refer to the instant compound. They are thus not disclosed as useful together, and have different modes of operation, different functions, and different effects. Finally, it is a burden to search and examine Groups involving both compounds and methods which are not used together in a disclosed method, and further because the searches are divergent and do not overlap. Restriction is considered proper therefore.

Inventions X and XIII are related as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product (MPEP § 806.05(h)). In the instant case the probes or oligonucleotides of Group X can be used to probe for the presence of the RNase HII transcript. Furthermore, it is a burden to search and examine Groups that are drawn to materially different entities (i.e. methods and compounds), because one contains an active process while the other is defined by its structure, and further because the searches are divergent and do not necessarily overlap. Restriction is considered proper therefore.

4. Regarding those Groups above indicating that election of a single sequence is required, each sequence is considered to comprise a patentably distinct invention for the following reasons. Although the RNase HI and HII sequences of Groups I and II catalyze similar reactions, and the antisense sequences targeted to RNase HII of Group XII each target and modulate expression of the same gene, all such sequences are considered to be unrelated to each other, since each RNase HII sequence and each antisense sequence claimed is structurally and

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functionally independent and distinct because each sequence has a unique nucleotide sequence. Furthermore, each antisense sequence targets a different and specific region of RNase HII, and each antisense oligo, upon binding to RNase HII, functionally modulates (increases or decreases) the expression of the gene and to varying degree (per applicants' Table 1 and 2 in the specification). Furthermore, a search of more than one (1) of the sequences claimed presents an undue burden on the Patent and Trademark Office due to the complex nature of the search and corresponding examination of more than one (1) of the claimed sequences. In view of the foregoing, should applicants elect one of Groups I, II, or XII, one (1) sequence from the elected Group is considered to be a reasonable number of sequences for examination.

### ***Conclusion***

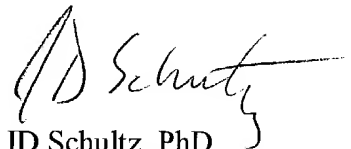
5. Applicant is advised that the reply to this requirement to be complete must include an election of the invention to be examined even though the requirement be traversed (37 CFR 1.143).
6. Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a request under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).
7. Any inquiry concerning this communication or earlier communications from the examiner should be directed to J. Douglas Schultz whose telephone number is 703-308-9355. The examiner can normally be reached on 8:00-4:30 M-F.

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If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, John L. LeGuyader can be reached on 703-308-0447. The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

JDS

A handwritten signature in black ink, appearing to read "JD Schultz", with a stylized flourish extending from the end.

JD Schultz, PhD  
Patent Examiner  
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